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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
10/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,950	RADTKEY ET AL.	
	Examiner	Art Unit	
	FRANK W. LU	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-14,18-23 and 25* is/are pending in the application.

4a) Of the above claim(s) *10-14 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-9,18-20,22,23 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of RCE and the amendment filed on July 16, 2008 have been entered. The claims pending in this application are claims 1, 6-14, 18-23, and 25 wherein claims 10-14 and 21 have been withdrawn due to species election mailed on July 16, 2008. Therefore, claims 1, 6-9, 18-20, 22, 23, and 25 will be examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 25 is rejected as vague and indefinite. Since claim 25 does not require that unlabeled blocker can specifically identify a polymorphism of cystic fibrosis while a detectable discriminator can specifically identify another polymorphism of cystic fibrosis, it is unclear why the method of claim 25 can be used to detect a polymorphism of cystic fibrosis. Please clarify.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 6-9, 18-20, 22, 23, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nerenberg *et al.,* (US 2001/0014449 A1, published on August 16, 2001) in view of Lannuzzi *et al.,* (Am. J. Hum. Genet., 48, 227-231,1991).

Regarding claim 1, Nerenberg *et al.,* teach providing patient sample nucleic acids containing a first and a second locus having a first and second polymorphisms (ie., amplicon 42 in Figure 4a) at a microarray site (ie., the electronically addressable microchip); providing an unlabeled blocker (ie., stabilizer probe 41 in Figure 4a) that is complementary to the first locus (ie., the region of amplicon 42 that is complementary to both reporter probes 41 and 44) containing the first polymorphism (ie., in the region of amplicon 42 that is complementary to reporter probe 44), hybridizing the unlabeled blocker with the first locus wherein the second

locus is unblocked; providing a detectable discriminator (ie., reporter probe 43 in Figure 4a) that is capable of hybridizing with the second locus containing the second polymorphism (ie., the region amplicon 42 that is complementary to reporter probe 43); hybridizing the detectable discriminators with the second locus containing the second polymorphism; and detecting the second polymorphism by detecting the presence of the discriminator at the microarray site (see abstract, pages 3-5, [0025] to [0045], claims 1-34 in pages 15-18, and Figure 4a and 4b).

Regarding claims 6 and 22, since Nerenberg *et al.,* teach that the capture sites in column 1 and 2 of the microchip receive a Hemochromatosis wild type and Factor V mutant while the sites in column 4 and 5 of the microchip are targeted with both Hemochromatosis and Factor V Heterozygotes, reporting is done sequentially, first with the allele-specific Hemochromatosis reporters (SEQ ID Nos. 11 and 12) and then the allele-specific Factor V reporters (SEQ ID Nos. 16 (CGCCTGTCCAG-CR6G) and 17 (TGCCTGTCCAG-Far Red), and before Factor V reporters are passively hybridized, all remaining Hemochromatosis reporters are stripped from the microarray (see page 7, [0058], page 11, [0100] to [0103], and claims 23 and 25 in page 17), Nerenberg *et al.,* disclose that the microarray site comprises a site of an actively addressable electronic microarray as recited in claim 6 and the multiple patient samples (ie., Hemochromatosis wild type, Factor V mutant, and Hemochromatosis and Factor V Heterozygotes) are provided on multiple sites (ie., columns 1, 2, 4, and 5 in [0102]) of the microarray as recited in claim 22.

Regarding claim 7, Nerenberg *et al.,* teach that the addressable electronic microarray includes a permeation layer (see page 7, [0059] and Figures 1A and 1B).

Regarding claims 8 and 9, Nerenberg *et al.,* teach that the patient sample is amplified as recited in claim 8 wherein the amplification includes polymerase chain reaction (PCR) as recited in claim 9 (see claims 1 and 2 in pages 15 and 16).

Regarding claim 18, Nerenberg *et al.,* teach performing a screening step (ie., analyzing unknown hemochromatosis samples) (see page 11, [0096] to [0099]).

Regarding claims 19 and 20, Nerenberg *et al.,* teach that the patient sample nucleic acid comprises multiple segments containing different loci (ie., the sites that two reporter probes 43 and 44 hybridize to) as recited in claim 19 wherein the multiple segments containing different loci are affixed to the same microassay site (ie., the site on the microchip) as recited in claim 20 (see page 12, [0111] and [0112], and Figures 4a and 4b).

Regarding claim 23, Nerenberg *et al.,* teach providing a labeled amplification control (ie., labeled reporter probe 44 in Figure 4a) that is capable of binding with the patient nucleic acid sample; and hybridizing the labeled amplification control to the patient nucleic acid sample (see Figure 4a and page 17, claim 30).

Nerenberg *et al.,* do not disclose that the patient sample nucleic acids contain a first and a second locus having first and second polymorphisms which are related to a genetic disease as recited in claim 1 wherein the genetic disease is cystic fibrosis as recited in claim 25. Although Figures 4a of Nerenberg *et al.,* does not teach that stabilizer probe 41 (ie., the unlabeled blocker in claim 1) blocks the first polymorphism (ie., the polymorphism in Figure 4a which is blocked by reporter probe 44), since Nerenberg *et al.,* teach the SNP base of amplicons is complementary to either the 3' base of the stabilizer/capture or the 5' base of the reporter probe (see page 4, [0031]), in view of the prior art of Nerenberg *et al.,* it would have been obvious to one having

ordinary skill in the art at the time the invention was made to have modified stabilizer probe 41 and reporter probe 44 by optimization of the lengths of stabilizer probe 41 and reporter probe 44 such that the first polymorphism (ie., the polymorphism in Figure 4a which is blocked by reporter probe 44) is blocked by 3' base of the unlabeled blocker (ie., stabilizer 41) as recited in claim 1 and is not blocked by reporter probe 44. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05). Although the examples in Figure 4a are used to identifying SNPs in the Mannose Binding Protein gene locus that correlates with susceptibility to sepsis in leukopenic patients and SNPs in the human HLA locus (see page 12, [0111] and [0112]), Nerenberg *et al.,* teach that "the number of loci required for any particular test on the array vary depending on the application, with generally one for genetic disease analysis, one to five for tumor detection, and six, eight, nine, thirteen or more for paternity testing and forensics" (see pages 7 and 8, [0063]) and the method taught by Nerenberg *et al.,* is used for "disease diagnostics, such as for the identification of polymorphisms in structural genes, regulatory regions, antibiotic or chemotherapeutic resistance conferring regions, or for SNPs associated with speciation or used for determination of genetic linkage" (see abstract) and "the accurate detection of diseased states, especially clonal tumor disease states, neurological disorders and predisposition to genetic disease" (see page 5, [0044] and [0045]).

Lannuzzi *et al.,* teach that a patient sample nucleic acids (ie., a patient sample comprising cystic fibrosis gene) contain a first and a second locus having first and second polymorphisms (ie., mutations in resides CF1154TC and ΔF508) which are related to a genetic disease as recited in claim 1 wherein the genetic disease is cystic fibrosis as recited in claim 25 (see page 230, left column).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 1 wherein the patient sample nucleic acids contain a first and a second locus having first and second polymorphisms which are related to a genetic disease such as cystic fibrosis in view of the prior art of Nerenberg *et al.,* and Lannuzzi *et al.*. One having ordinary skill in the art would have been motivated to do so because Nerenberg *et al.,* teach that "the number of loci required for any particular test on the array vary depending on the application, with generally one for genetic disease analysis, one to five for tumor detection, and six, eight, nine, thirteen or more for paternity testing and forensics" (see pages 7 and 8, [0063]) and the method taught by Nerenberg *et al.,* is used for "disease diagnostics, such as for the identification of polymorphisms in structural genes, regulatory regions, antibiotic or chemotherapeutic resistance conferring regions, or for SNPs associated with speciation or used for determination of genetic linkage" (see abstract) and "the accurate detection of diseased states, especially clonal tumor disease states, neurological disorders and predisposition to genetic disease" (see page 5, [0044] and [0045]). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the method recited in claim 1 using patient sample

nucleic acids containing a first and a second locus having first and second polymorphisms which are related to a genetic disease such as cystic fibrosis.

Response to Arguments

In page 5, second paragraph bridging to page 6, last paragraph of applicant's remarks, applicant argues that Nerenberg *et al.,* do not teach hybridizing the unlabeled blocker with the first locus such that the first polymorphism is blocked by the unlabeled blocker as recited in claim 1.

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because the examiner has adjusted above rejection. Although Figures 4a of Nerenberg *et al.,* does not teach that stabilizer probe 41 (ie., the unlabeled blocker in claim 1) blocks the first polymorphism (ie., the polymorphism in Figure 4a which is blocked by reporter probe 44), since Nerenberg *et al.,* teach the SNP base of amplicons is complementary to either the 3' base of the stabilizer/capture or the 5' base of the reporter probe (see page 4, [0031]), in view of the prior art of Nerenberg *et al.,* it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have modified stabilizer probe 41 and reporter probe 44 by optimization of the lengths of stabilizer probe 41 and reporter probe 44 such that the first polymorphism (ie., the polymorphism in Figure 4a which is blocked by reporter probe 44) is blocked by 3' base of the unlabeled blocker (ie., stabilizer 41) as recited in claim 1 and is not blocked by reporter probe 44. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or

workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05).

Conclusion

7. No claim is allowed.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

/Frank W Lu /
Primary Examiner, Art Unit 1634
October 8, 2008